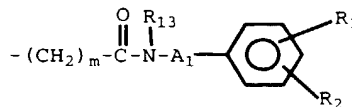


What is claimed is:

1. A diagnostic agent comprising an aminocarboxylate ligand complexed with a paramagnetic metal ion wherein a nitrogen atom within said  
5 aminocarboxylate is substituted with a substituted aromatic amide group.

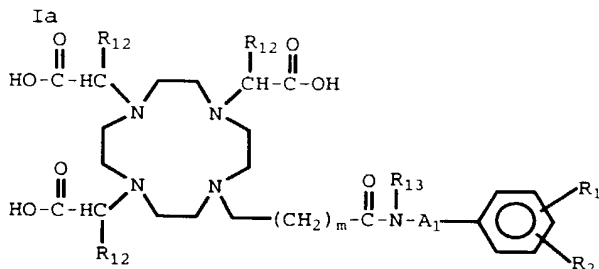
2. The diagnostic agent of claim 1 wherein said substituted aromatic amide group is of the formula

10 I

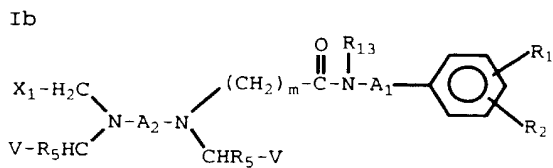


wherein

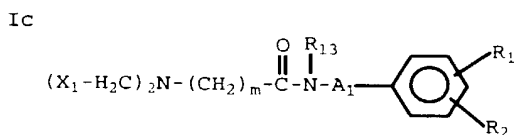
A<sub>1</sub> is -(CH<sub>2</sub>)<sub>m'</sub>- or a single bond;  
15 (CH<sub>2</sub>)<sub>m</sub> and (CH<sub>2</sub>)<sub>m'</sub> may independently be substituted with alkyl or hydroxyalkyl;  
R<sub>1</sub> and R<sub>2</sub> are each independently hydrogen, alkyl, -NO<sub>2</sub>, -NH<sub>2</sub>,  $-\overset{\overset{S}{\parallel}}{N}H-C-NH-R_{12}$ , NCS,  $-\overset{\overset{O}{\parallel}}{C}-NR_3R_4$ , NR<sub>3</sub>COR<sub>9</sub>,  
20 where R<sub>9</sub> is alkyl or hydroxyalkyl, with the proviso that at least one of R<sub>1</sub> and R<sub>2</sub> must be other than hydrogen;  
R<sub>3</sub> and R<sub>4</sub> are independently hydrogen, alkyl, arylalkyl, aryl, alkoxy and hydroxyalkyl;  
R<sub>12</sub> is hydrogen, alkyl or hydroxyalkyl;  
25 R<sub>13</sub> is hydrogen, alkyl, arylalkyl, alkoxy or hydroxyalkyl;  
m and m' are independently 1 to 5;  
and multimeric forms thereof.



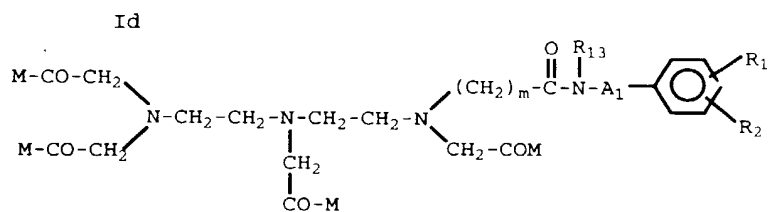
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10



15



wherein  $m$ ,  $R_{13}$ ,  $A_1$ ,  $R_1$ ,  $R_2$ , and  $R_{12}$  are as defined in claim 2 and wherein

$X_1$  is  $-COOY_1$ ,  $PO_3HY_1$  or  $-CONHOY_1$ ;

$Y_1$  is a hydrogen atom, a metal ion equivalent and/or a physiologically biocompatible cation of an inorganic or organic base or amino acid;

5  $A_2$  is  $-CHR_6-CHR_7-$ ,  $-CH_2CH_2(ZCH_2-CH_2)_n-$ ,  
 $N(CH_2X_1)_2$   $CH_2-CH_2-N(CH_2X_1)_2$   
 $-CH_2-\underset{\substack{| \\ N(CH_2X_1)_2}}{CH}-CH_2$  or  $-CH_2-CH_2-\underset{\substack{| \\ N(CH_2X_1)_2}}{N}-CH_2-CH_2-$ , wherein  
 $X_1$  is as defined above;

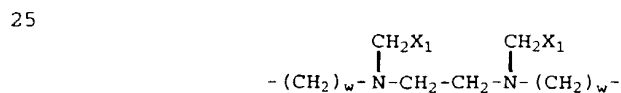
each  $R_5$  is hydrogen or methyl;

10  $R_6$  and  $R_7$  together represent a trimethylene group or a tetramethylene group or individually are hydrogen atoms, lower alkyl groups (e.g., 1-8 carbons), phenyl groups, benzyl groups or  $R_6$  is a hydrogen atom and  $R_7$  is  $-(CH_2)_p-C_6H_4-W$ -protein where  $p$  is 0 or 1,  $W$  is  $-NH-$ ,  $-NHCOCH_2-$  or  $-NHCS-$ , protein  
15 represents a protein residue;

$n$  is 1, 2 or 3;

$Z$  is an oxygen atom or a sulfur atom or the group  $NCH_2X_1$  or  $NCH_2CH_2OR_8$  wherein  $X_1$  is as defined above and  $R_8$  is  $C_1$ -8alkyl;

20  $V$  is  $X_1$  or is  $-CH_2OH$ ,  $-CONH(CH_2)_rX_1$  or  $-COB$ , wherein  $X_1$  is as defined above,  $B$  is a protein or lipid residue,  $r$  is an integer from 1 to 12, or if  $R_5$ ,  $R_6$  and  $R_7$  are each hydrogen; then both  $V$ 's together form the group



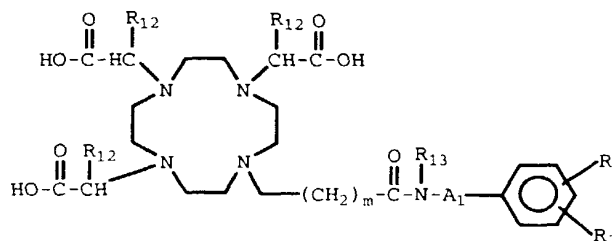
where  $X_1$  is as above,  $w$  is 1, 2 or 3, provided that  
30 at least two of the substituents  $Y_1$  represent metal ion equivalents of an element with an atomic number of 21 to 29, 42, 44 or 57 to 83; from 1 to 4, advantageously 2 or 3, and preferably 2  $M$ 's are  $-OH$  and the balance independently are  $-OR_{10}$ ,  $-NH_2$ ,

-NHR<sub>10</sub> and/or NR<sub>10</sub>R<sub>10</sub>' wherein R<sub>10</sub> and R<sub>10</sub>' are selected from an organic alkyl radical of up to 18 carbon atoms which may be substituted.

4. The diagnostic agent of claim 1 wherein said paramagnetic metal ion is gadolinium.

5. A compound of formula Ia, Ib, Ic or Id as defined in claim 3, including multimers thereof.

6. A compound of the formula



wherein

A<sub>1</sub> is -(CH<sub>2</sub>)<sub>m</sub>'- or a single bond;

(CH<sub>2</sub>)<sub>m</sub> and (CH<sub>2</sub>)<sub>m</sub>' may independently be substituted with alkyl or hydroxyalkyl;

R<sub>1</sub> and R<sub>2</sub> are each independently hydrogen,

alkyl, -NO<sub>2</sub>, -NH<sub>2</sub>, -NHCNHR<sub>12</sub>, NCS, -C(=O)-NR<sub>3</sub>R<sub>4</sub> and NR<sub>3</sub>COR<sub>9</sub> where R<sub>9</sub> is alkyl or hydroxyalkyl, with the proviso that at least one of R<sub>1</sub> and R<sub>2</sub> must be other than hydrogen;

R<sub>3</sub> and R<sub>4</sub> are independently hydrogen, alkyl, arylalkyl, aryl, alkoxy and hydroxyalkyl;

R<sub>12</sub> is hydrogen, alkyl or hydroxyalkyl;

R<sub>13</sub> is hydrogen, alkyl, arylalkyl, aryl, alkoxy or hydroxyalkyl;

m and m' are independently 1 to 5;

and multimeric forms thereof.

7. A compound of claim 6 wherein  $R_1$  and  $R_2$

are each  $\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{NR}_3\text{R}_4 \end{array}$  wherein each  $\text{R}_3$  group is hydroxy-alkyl.

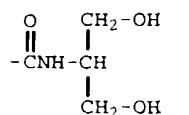
8. A compound of claim 6 wherein R<sub>1</sub> and R<sub>2</sub>

5 are each  $\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{NR}_3\text{R}_4 \\ | \\ -\text{CH}_2-\text{CH}-\text{CH}_2\text{OH} \\ | \\ \text{OH} \end{array}$  wherein each  $\text{R}_3$  group is selected from  $\text{OH}$  and  $-\text{CH}(\text{CH}_2\text{OH})_2$ , and wherein each  $\text{R}_4$  group is hydrogen.

9. A compound of claim 6 wherein R<sub>1</sub> and R<sub>2</sub>

are each  $\begin{array}{c} \text{O} \quad \text{OH} \\ \parallel \quad | \\ \text{---CNHCH}_2\text{---CH---CH}_2\text{---OH} \end{array}$

10            10. A compound of claim 6 wherein R<sub>1</sub> and R<sub>2</sub>  
are each



11 A compound of claim 6 having the name

15 10-[2-([3,5-bis([(2,3-dihydroxypropyl)amino]-  
carbonyl]phenyl)amino)-2-oxoethyl]-1,4,7,10-  
tetraazacyclododecane-1,4,7-triacetic acid.

12. The gadolinium complex of the compound of claim 11.

20 13. A compound of claim 6 having the name  
10-[2-[[3,5-bis-[[[2-hydroxy-1-(hydroxymethyl)-  
ethyl]amino]carbonyl]phenylamino]2-oxoethyl]-  
1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

14. The gadolinium complex of the compound of  
25 claim 13.

15. A compound of claim 6 having the name  
10-[2-[methyl[3,5-bis[[ (2-methylbutyl)amino]-

carbonyl]phenyl]amino]-2-oxoethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

16. The gadolinium complex of the compound of claim 15.

5 17. A compound of claim 6 having the name 10-[2-[[4-[[2,3-dihydroxypropyl]amino]carbonyl]-phenyl]amino]-2-oxoethyl-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

10 18. The gadolinium complex of the compound of claim 17.

19. A compound of claim 6 having the name 10-[N-(4-nitrophenyl)acetamido]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

15 20. The gadolinium complex of the compound of claim 19.

21. A compound of claim 6 having the name 10-[N-(4-aminophenyl)acetamido]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

20 22. The gadolinium complex of the compound of claim 21.

23. A compound of claim 6 having the name 10-[[N-(4-(N'-isothiocyanato)phenyl)acetamido]]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

25 24. The gadolinium complex of the compound of claim 23.

25. A compound of claim 6 having the name 10-[N-[4-(N'-methylthioureido)phenyl]acetamido]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

30 26. The gadolinium complex of the compound of claim 25.

27. A compound of claim 6 having the name 10-[N-[4-(N',N'-diethylaminothioureido)phenyl]-acetamido]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

29. A compound of claim 6 having the name 10,10'-[[[[[(1,2-ethanediyl)diimino]bis(thioxomethyl)-diimino]bis(4,1-phenylene)]diimino-bis[1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid]].

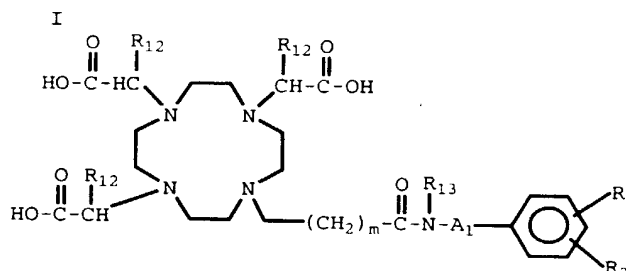
31. A compound of claim 6 having the name  
10,10'-[{{{(Thioxomethyl)bis(imino)bis(4,1-  
phenylene)}bis(imino)}bis(2-oxo-2,1-ethanediyl)]-  
1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

33. A compound of claim 6 having the name  
10,10',10''-[[[[[[iminobis(2,1-ethanediyl)triimino]-  
tris(thioxomethyl)]-triimino]tris-(4,1-phenylene)]-  
triimino]tris(2-oxo-2,1-ethanediyl)]tris[1,4,7,10-  
tetraazacyclododecane-1,4,7-triacetic acid].

35. A compound of claim 6 having the name 10-[2-[[2-(4-nitrophenyl)ethyl]amino]-2-oxoethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

37. A compound of claim 6 having the name 10-[2-[[3,5-bis[[ (2-hydroxyethyl)amino]-carbonyl]-phenyl]amino]-2-oxoethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid, monosodium salt.

38. The gadolinium complex of the compound of claim 37.



A<sub>1</sub> is -(CH<sub>2</sub>)<sub>m</sub>'- or a single bond;

$(\text{CH}_2)_m$  and  $(\text{CH}_2)_{m'}$  may independently be

10 substituted with alkyl or hydroxyalkyl;

$R_1$  and  $R_2$  are each independently hydrogen,

alkyl,  $-\text{NO}_2$ ,  $-\text{NH}_2$ ,  $-\text{NHC}(=\text{S})\text{NHR}_{12}$ ,  $\text{NCS}$ ,  $-\text{C}(=\text{O})-\text{NR}_3\text{R}_4$  and  $\text{NR}_3\text{COR}_9$  where  $\text{R}_9$  is alkyl or hydroxyalkyl, with the proviso that at least one of  $\text{R}_1$  and  $\text{R}_2$  must be other than hydrogen;

R<sub>3</sub> and R<sub>4</sub> are independently hydrogen, alkyl, arylalkyl, aryl, alkoxy and hydroxyalkyl;

R<sub>12</sub> is hydrogen, alkyl or hydroxyalkyl;

R<sub>13</sub> is hydrogen, alkyl, arylalkyl, aryl,

20           alkoxy or hydroxyalkyl;

$m$  and  $m'$  are independently 1 to 5;

and multimeric forms thereof.

40. A complex of claim 39 wherein  $R_1$  and  $R_2$

are each  $\text{-}\overset{\text{O}}{\parallel}\text{C-NR}_3\text{R}_4$  wherein each  $\text{R}_3$  group is hydroxy-  
25 alkyl.

41. A complex of claim 39 wherein R<sub>1</sub> and R<sub>2</sub> are each  $\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{NR}_3\text{R}_4 \\ | \\ \text{OH} \end{array}$  wherein each R<sub>3</sub> group is selected from  $-\text{CH}_2-\text{CH}-\text{CH}_2-\text{OH}$  and  $-\text{CH}(\text{CH}_2\text{OH})_2$ , and wherein each R<sub>4</sub> group is hydrogen.

5            42. A complex of claim 39 wherein R<sub>1</sub> and R<sub>2</sub>  
                O          OH  
                ||        |  
 are each -CNHCH<sub>2</sub>-CH-CH<sub>2</sub>-OH

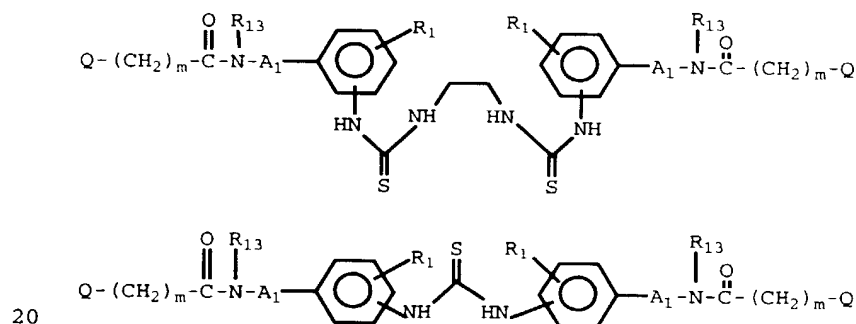
43. A complex of claim 39 wherein  $R_1$  and  $R_2$  are each

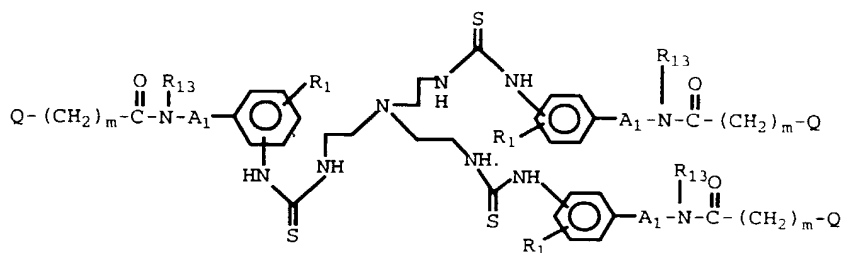


44. A complex of claim 39 wherein said metal atom is of atomic number 56-83.

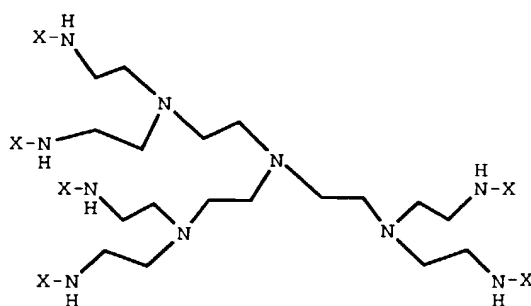
45. A complex of claim 39 wherein said metal  
15 is gadolinium(III).

46. A multimer selected from

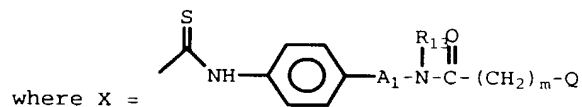




or



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and wherein Q is an aminocarboxylate ligand and the other variables are as defined in claim 3.

47. A compound of claim 6 having the name 10-[2-[[3,5-bis((2-methylbutyl)amino)carbonyl]-phenyl]amino]2-oxoethyl]1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

48. The gadolinium complex of the compound of claim 47.

49. A compound of claim 6 having the name 10,10',10'',10''',10'''',10'''''-[[[[[[[[[Nitrilo-

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50. The gadolinium complex of the compound of claim 49.